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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/805,804

03/22/2004

David C. Baulcombe

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EXAMINER

MEHTA, ASHWIN D

ART UNIT

PAPER NUMBER

1638

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	<b>Application No.</b> 10/805,804	<b>Applicant(s)</b> BAULCOMBE ET AL.	
	<b>Examiner</b> Ashwin Mehta	<b>Art Unit</b> 1638	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 29 September 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
 b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
 (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
 (b) ☐ They raise the issue of new matter (see NOTE below);  
 (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
 5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
 6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
 7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
 The status of the claim(s) is (or will be) as follows:  
 Claim(s) allowed: \_\_\_\_\_.  
 Claim(s) objected to: \_\_\_\_\_.  
 Claim(s) rejected: \_\_\_\_\_.  
 Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
 12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.  
 13. ☐ Other: \_\_\_\_\_.

/Ashwin Mehta/  
 Primary Examiner, Art Unit 1638

Continuation of 11. does NOT place the application in condition for allowance because: Claims 125-130 remain rejected under 35 U.S.C. 102(e) as being anticipated by Graham (U.S. Patent No. 6,573,099, issued June 3, 2003, filed June 19, 1998), for the reasons of record stated in the previous Office actions. Applicants traverse in the papers filed September 29, 2008. Applicants' arguments were fully considered but were not persuasive. Applicants argue that Graham never describes constructs that contain DNA sequences that will transcribe into molecules of 20-24 nucleotides. Applicants point to column 5, lines 7-20, and interpret this passage as requiring a minimum of at least 30 nucleotides to be transcribed from the constructs of Graham. Applicants request that any location in the reference that shows that RNAs of 30 nucleotides, let alone 20-30 nucleotides, are said to be produced, be identified (response, pages 8-9). However, that the sequences of the reference be a minimum of 30 nucleotides is apparently not a requirement. Column 6, lines 25-27 do indicate that it can comprise 20-30 nucleotides. Applicants argue that the statements in column 6 must be reconciled with the requirement set forth in column 5, that the statements can be consistent only if one interprets them as referring to portions of the required 30 nucleotide sequences derived from the target gene. However, Graham does not teach such an interpretation. Applicants argue that even if the Office's interpretation is correct, that the present claims are still not anticipated, that Graham does not teach constructs within this size range. Applicants argue there is no specific disclosure of producing RNA molecules of 20-24 nucleotides, not even inherently (response, pages 10-12). However, as the produced RNA molecule can be 20-30 nucleotides in length, one can at once envisage each of the lengths that lie between 20-30.

Claims 116-124 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al. (U.S. Patent No. 6,506,559, issued January 14, 2003, filed December 18, 1998) in view of Graham (U.S. Patent No. 6,573,099, issued June 3, 2003, filed June 19, 1998), for the reasons of record stated in the previous Office actions. Applicants traverse in the papers filed September 29, 2008. Applicants' arguments were fully considered but were not persuasive. As in previous responses, Applicants argue that Fire teaches away from RNA molecules even as short as 25 nucleotides (response, page 13). Applicant's arguments are not found persuasive, for the reasons discussed in the previous Office action. Applicants argue that there was a known problem at the time of the Fire and Graham priority dates, with using long dsRNA in vertebrate or mammalian systems, that they induce an interferon response resulting in non-specific destruction of mRNAs. Applicants ask that, given this, if it were obvious at the time that SRMs would have avoided this effect, why did neither Graham nor Fire confirm the existence of such molecules as was done by the present inventors, and why did they not disclose use of this size of molecules (response, pages 13-14)? However, it should be noted that it is the elected species of plants that is being examined. This interferon response does not occur in plants. Applicants argue that Graham does not remedy the deficiency of Fire that the length of the RNA molecules is not specifically taught, citing the arguments above regarding Graham (response, pages 14-15). This is not found persuasive for the reasons discussed above. Applicants argue that Graham is devoid of suggestions as to what might be required should the RNA be supplied to cells directly, that there is no reason to believe that the size requirements would be the same in both cases (response, page 15). However, no reasons for this position are provided.

Claims 116-130 remain under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 6,723,897, issued April 20, 2004, filed August 19, 1999), for the reasons of record stated in the previous Office actions. Applicants traverse in the papers filed September 29, 2008. Applicants' arguments were fully considered but were not persuasive. Applicants argue that Brown merely mentions cosuppression without further description, so it is speculative as to what is being associated with that length. In apparent reference to the previous Office action, Applicants argue that they do not agree that the presence of the recitation, "such as by" before "antisense expression" (in column 3, lines 58-67) results in the implication that the sizes specified apply to molecules used for cosuppression. Applicants argue that if the minimum requirement is 12 contiguous nucleotides, this is smaller than what is required by Fire or Graham (response, page 16). However, Brown does not state that it is "required" for the RNA molecules to be 12 contiguous nucleotides, other sizes are recited. Further, neither Fire nor Graham are included in this rejection. Applicants also argue that Brown, in the passage in question in col. 3, lists other methods for reducing expression, and that this length description cannot apply to all of the methods set forth earlier in the paragraph (response, page 16). However, clearly the length descriptions can apply to molecules used for cosuppression. Applicants continue, arguing that every single time sequences of a specified length are discussed in Brown it is antisense RNA that is referred to. Applicants point to col. 5, lines 50-60, as describing the length of antisense constructs (response, page 16). However, in this passage, again, antisense is referred to only as an example. This passage indicates that nucleic acid segments of recited sequence identifiers, and their complements, are contemplated to be compositions of the invention. This includes sense sequences. Applicants also argue that the specific range of 20-24 nucleotides is clearly not suggested by Brown, that Brown mentions a range of 12 nucleotides to full length encoding sequences, that the Office appears to have overlooked the teaching of the present invention which requires that the RNA be between 20 and 24 nucleotides (response, page 17). However, the rejection did not indicate that the RNA must be 12 nucleotides in length, but rather points out that Brown does include nucleotides lengths of at least 20 nucleotides, and even recites specifically that it may be at least 20 or at least 24, and therefore would have been obvious to make fragment sizes to be 20, 21, 22, 23, or 24 nucleotides long, as this is within the size range taught by Brown et al.